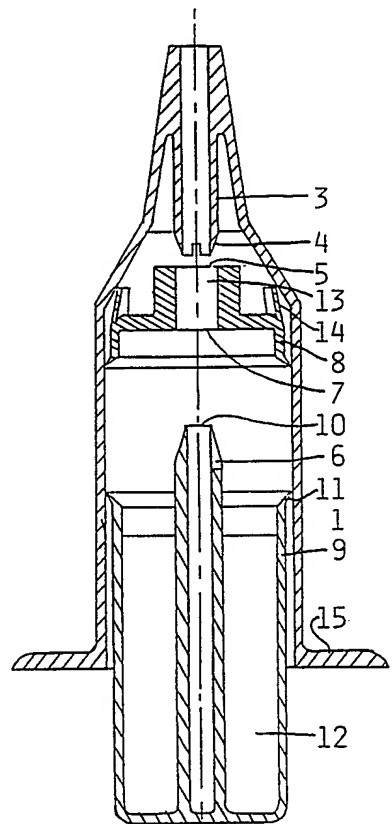


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : A61M 15/00	A1	(11) International Publication Number: WO 93/11818 (43) International Publication Date: 24 June 1993 (24.06.93)
(21) International Application Number: PCT/DK92/00373 (22) International Filing Date: 10 December 1992 (10.12.92) (30) Priority data: 1985/91 10 December 1991 (10.12.91) DK (71) Applicant: NOVO NORDISK A/S [DK/DK]; Novo Allé, DK-2880 Bagsvaerd (DK). (72) Inventors: ELK, Svend ; Lyngborghave 48, DK-3460 Birkeroed (DK). STEENGAARD, Kim ; Ketilstorp Allé 53, DK-2650 Hvidovre (DK). KOSTER, Hans ; Helsebakken 5, DK-2900 Hellerup (DK). (74) Common Representative: NOVO NORDISK A/S; Patent Department, EiT, Novo Allé, DK-2880 Bagsvaerd (DK).		(81) Designated States: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, UA, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: DISPOSABLE DISPENSER FOR DRUGS (57) Abstract <p>A dispenser for dispensing a dosage or a powdery or fluid drug from a cartridge having a tubular chamber (13) the ends of which are sealed by breakable membranes (5, 7). The dispenser comprises a housing (1) forming a cylinder which is at one end closed by an end wall through which an outlet pipe (3) communicates with the interior of the cylinder. The other end of the cylinder is closed by a plunger (9) which may be displaced into the cylinder. The drug cartridge is placed in a piston (8) mounted axially displaceable in the cylinder between the end wall and the plunger (9), and the tubular chamber (13) extends from one side of the piston (8) to the other. Penetrators (4, 10) for breaking the membranes (5, 7) are provided at the inner end of the outlet pipe (3) and at the inner end of the plunger (9).</p> <div style="text-align: right;">  </div>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	MR	Mauritania
AU	Australia	GA	Gabon	MW	Malawi
BB	Barbados	GB	United Kingdom	NL	Netherlands
BE	Belgium	GN	Guinea	NO	Norway
BF	Burkina Faso	GR	Greece	NZ	New Zealand
BG	Bulgaria	HU	Hungary	PL	Poland
BJ	Benin	IE	Ireland	PT	Portugal
BR	Brazil	IT	Italy	RO	Romania
CA	Canada	JP	Japan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SK	Slovak Republic
CI	Côte d'Ivoire	LI	Liechtenstein	SN	Senegal
CM	Cameroon	LK	Sri Lanka	SU	Soviet Union
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	MC	Monaco	TG	Togo
DE	Germany	MG	Madagascar	UA	Ukraine
DK	Denmark	ML	Mali	US	United States of America
ES	Spain	MN	Mongolia	VN	Viet Nam
FI	Finland				

DISPOSABLE DISPENSER FOR DRUGS

The invention concerns a disposable dispenser for drugs, and more specifically a dispenser for dispensing a dosage of a powdery or fluid drug stored in a cartridge having a tubular chamber, the ends of which are sealed by breakable
5 membranes.

Such dispensers may be used for dispensing powdery medicine which can be absorbed through the nasal mucous membranes and which is only given occasionally, e.g. emergency administration of glucagon for treating hypoglycaemic diabetics. Therefore, the dispenser should be suited for storing an appropriate
10 dosage of a drug and should be easily operated to administer this dosage as a cloud of particles or droplets even by unprofessionals when necessary.

US 2,672,144 discloses a disposable powder dispenser having the powdery drug stored in a bottle shaped vessel also containing a charge of compressed gas and sealed at the end of the bottle neck with a sealing which may
15 be broken by a penetrator when the vessel is pressed into the dispenser unit. By using this dispenser care must be taken to ensure that the powder is passed up into the bottle neck - a precaution which cannot be expected to be taken by unprofessionals in an emergency situation. Further, the compressed gas may leak during storage, and consequently the dispenser may be unusable when the
20 emergency situation occurs.

EP 407 276 discloses a dispenser having powder stored in a tubular chamber being closed at its air inlet end by a membrane and at its outlet end by a removable lid. Immediately before use the lid is removed before the outlet end is inserted in a nostril. However, unless the powder appears as a lump wedging in the
25 outlet, there will be a risk of spilling some of the powder, if the outlet should be inserted in the nostril of a person lying down. For the same reason, this dispenser is not usable for fluid drugs.

A dispenser wherein powder is stored in a tubular chamber, the ends of which are closed by penetrable membranes, is known from WO 91/06333. In this
30 dispenser a number of chambers are successively brought into alignment with an

air supply pipe and an outlet pipe, and the membranes closing the chamber are penetrated by penetrators at the ends of these pipes. However, according to the construction of the apparatus the membrane at the air supply end is first broken, and thereafter the membrane at the outlet is penetrated.

5 However, the penetrations are requested to take place in the opposite order to ensure that the outlet passage from the chamber to the nostril is opened before the chamber is opened to the pressurized air, but not until the outlet pipe is inserted in the nostril. If the membrane separating the chamber from the compartment with the pressurized air is broken first, a powder or a fluid may fall out of
10 the chamber into the compartment, as an air flow through the chamber is not established until both membranes are broken.

It is the object of the invention to provide a dispensing device which meets the above requests without involving the stated draw-backs of the dispensers according to the known art.

15 This is obtained by a dispenser comprising a housing forming a cylinder which is at one end closed by an end wall through which an outlet pipe communicates with the interior of the cylinder, the other end of the cylinder being closed by a plunger which may be operated to displace it axially into the cylinder towards the end wall, the dispenser being characterized in that the drug cartridge
20 is placed in a free piston mounted axially movably in the cylinder between the end wall and the plunger, the tubular chamber of the cartridge extending in the axial direction of the cylinder from one side of the piston to the other, and means for breaking the sealing membranes of the cartridge being provided at least at the inner end of the outlet pipe.

25 The operation of the dispenser according to the invention is very simple, as only the plunger has to be pressed into the cylinder. The air pressure thereby provided between the plunger and the piston will force the latter forwards in the cylinder towards the end wall until the membrane facing this wall abuts the membrane breaking means provided at the inner end of the outlet tube.

30 The membrane breaking means may be a penetrator having a diameter smaller than the diameter of the bore of the tubular chamber and a length longer

than the length of this chamber. Such a penetrator will first penetrate the membrane facing the end wall. When the piston is forced further towards the end wall of the cylinder, the penetrator will pass through the chamber and the drug to ultimately penetrate the membrane facing the plunger, this membrane being penetrated from
5 its side facing the interior of the chamber.

According to the invention, the membrane breaking means may comprise a penetrator at the mouth of the outlet tube and another penetrator at the inner end of the plunger. When the plunger is pressed into the cylinder, the magazine is by the air pressure provided pressed with its one membrane against the
10 penetrator at the outlet pipe. When the plunger is pressed further into the cylinder, the penetrator at the inner end of the plunger is pressed through the other membrane of the magazine. This embodiment ensures that the last membrane is not broken until the plunger is pressed home and the highest obtainable air pressure is provided.

15 To avoid that the membrane of the magazine is pressed against the penetrator at the mouth of the outlet tube during the mounting of the piston or due to an inadvertently minor push on the plunger resilient spacing, means may be provided between the piston and the end wall. When a sufficient pressure is provided in the compartment between the plunger and the piston, the resilient
20 means gives to allow the penetrator to penetrate the membrane.

The dispenser may be equipped with two outlet pipes, two chambers in the piston, and two sets of penetrators, each pipe, chamber, and penetrator set cooperating as in the monopipe solution. Thereby it is taken into account that a nostril may be blocked or may show a decreased capacity concerning assimilation
25 of the medicine.

In the following the invention will be further described referring to the drawing, wherein

Figure 1 shows a sectional view of an embodiment of a dispenser according to the invention, and
30 Figure 2 shows a sectional view of another embodiment of the dispenser.

Figure 3 shows the upper part of an embodiment of a dispenser having two outlet pipes.

An embodiment of the dispenser as shown in Figure 1 comprises a housing 1 forming a cylinder which is at one end closed by an end wall through which an outlet pipe 3 communicates with the interior of the cylinder. Into the other end of the cylinder a plunger 9 is air tightly fitted forming along its perimeter a lip 11 enhancing the sealing with increasing pressure in the cylinder. The plunger is provided with an air pocket 12 to limit the maximum pressure when the plunger is pressed into the cylinder.

10 In the cylinder between the end wall and the plunger 9, a piston 8 is placed which is freely displaceable in the cylinder. An axial bore through the piston 8 forms a tubular chamber 13 which is at its ends closed by penetrable upper and lower membranes 5 and 7, respectively. The chamber 13 contains the powdery or fluid drug to be dispensed.

15 When the plunger 9 is pressed into the cylinder, the air pressure provided between the plunger 9 and the piston 8 will make the latter move axially towards the end wall. Resilient members 14 are provided on the top of the piston 8 to keep it at some distance from the end wall and a penetrator 4 provided at the inner end of the outlet pipe 3, until the pressure at the plunger side of the piston 8 is sufficiently high to bend these resilient members, so that the upper membrane 5 is broken by the penetrator 4. The resilient members 14 are provided to ensure that the membrane 5 is not inadvertently broken by the penetrator 4 during the mounting of the piston 8 or due to minor forces exerted on the plunger 9 before the intended use of the dispenser.

25 After the membrane 5 has been broken due to the pressure provided under the piston 8 pressing the membrane against the penetrator 4, the pressure in the chamber will rise as the plunger 9 is pressed further into the cylinder. When the plunger is pressed home, a penetrator 10 at the top of the plunger perforates the lower membrane 7 closing the chamber 13 and thereby opens for an air flow

from the compartment between the plunger 9 and the piston 8 through the chamber 13 and out through the outlet pipe 2.

Whereas the penetrator 4 is designed to form a sealing around the edge of the chamber 13 when the membrane 5 has been penetrated, the penetrator 5 10 penetrating the membrane 7 is designed to leave passages 6 communicating the chamber 13 with the compartment between the piston 8 and the plunger 9.

At the open end of the housing 1, finger grips 15 are provided the device being so dimensioned that the finger grips 15 may be gripped behind by the forefinger and the long finger, and the bottom of the plunger 9 may be pressed by 10 the thumb. When the outlet pipe 3 is placed in a patient's nostril the drug may be dispensed as a small cloud into the nostril by this simple gripping and pressing operation.

In the embodiment shown in Figure 2, all parts corresponding to the parts known from Figure 1 are given the same reference numbers. The only 15 difference is that the penetrator 4' is given another shape, and the penetrator 10 in Figure 1 is omitted.

The penetrator 4' has a length exceeding the length of the chamber 13. When the piston 8 is pressed forwards in the housing 1, the upper membrane 5 is first penetrated by the penetrator 4'. This penetrator has a diameter allowing it to 20 pass through the chamber 13 and subsequently penetrate the lower membrane 7 to open a discharge passage for the pressurized air between the piston 8 and the plunger 9. Instead of a penetrator the plunger 9 has a part 16 which may help to press the piston 8 against the penetrator 4' when the piston 8 is pressed home. This part 16 is provided with passages 6 which make space for the cutting edges of the 25 penetrator 4' and prevent the part 16 from sealing against the lower side of the piston 8.

In the shown embodiment, the penetrator 4' is a puncheon having a cross-shaped cross section and being sharpened at its front end. At its root the puncheon is provided with a means sealing along the upper edge of the chamber 30 13 immediately before the lower membrane 7 is punched.

It shall be noticed that the penetrators are so designed that no parts of the membranes are cut free to be entrained by the air discharged from the device. In Figure 1, this is obtained by a recess 2 in the cutting edge of the penetrator 4 leaving a string of the membrane 5 uncut when penetrated. In Figure 2, a cross shaped cut is made in the central part of the membrane 5, whereas the outer edge of the provided membrane sectors is still secured to the edge of the chamber.

As the assimilation capacity of the nostrils varies, it is impossible to know at forehand which nostril will be best suited for the administration of medicine. This problem may be overcome by adding medicine in both nostrils. For this purpose the dispenser in Figure 3 has been designed. Figure 3 shows the outlet end of the dispenser, which in this embodiment is equipped with two outlet tubes 3 each having a penetrator 4. The piston 8 has two chambers 13 aligned with the outlet tubes, and the not shown plunger has penetrators correspondingly aligned with the chambers 13 and the outlet tubes 3. This alignment may be obtained by the housing 15 1 having a cross section which is not circular, but rather oval.

CLAIMS

1. A dispenser for dispensing a dosage of a powdery or fluid drug stored in a cartridge having a tubular chamber the ends of which are sealed by breakable membranes, this dispenser comprising a housing forming a cylinder which
5 at one end is closed by an end wall through which an outlet pipe communicates with the interior of the cylinder, the other end of the cylinder being closed by a plunger having means to displace it axially into the cylinder towards the end wall, the dispenser being characterized in that the drug cartridge is placed in a piston mounted axially displaceably in the cylinder between the end wall and the plunger,
10 the tubular chamber of the cartridge extending in the axial direction of the cylinder from one side of the piston to the other, and means for breaking the sealing membranes of the cartridge being provided at least at the inner end of the outlet pipe.

2. A dispenser according to claim 1, **characterized** in, that the
15 membrane breaking means is provided as a cutting protrusion at the mouth of the outlet pipe inside the cylinder.

3. A dispenser according to claim 2, **characterized** in, that the protrusion has a diameter smaller than the diameter of the bore of the tubular chamber, and is longer than the length of this chamber.

20 4. A dispenser according to claim 1 or 2, **characterized** in, that a cutting member is provided at the inner side of the plunger, this cutting member being aligned with the facing membrane.

5. A dispenser according to any of the preceding claims, **characterized** in, that resilient spacing means is provided between the piston and the end wall.

6. A dispenser according to any of the preceding claims, characterized in, that two outlet pipes are provided, each pipe being allocated a chamber in the piston and penetrators for penetrating the membranes of the allocated chambers.

1/1

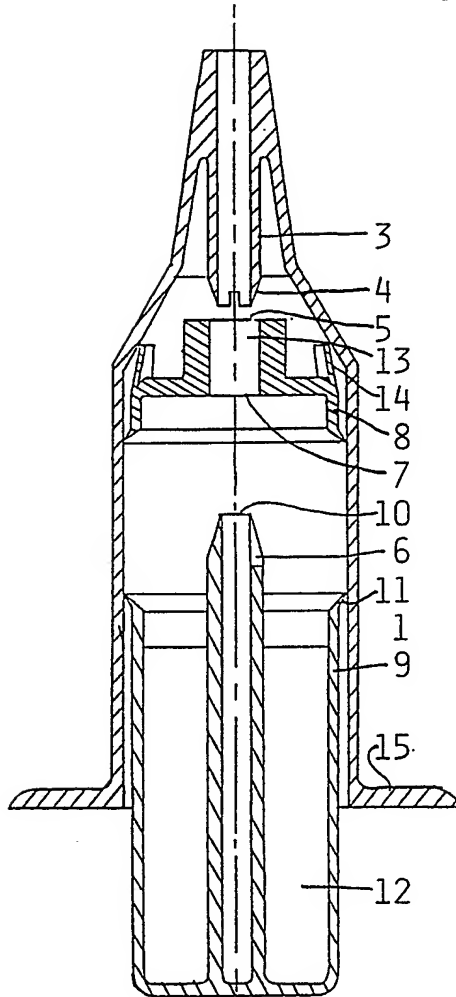


Fig. 1

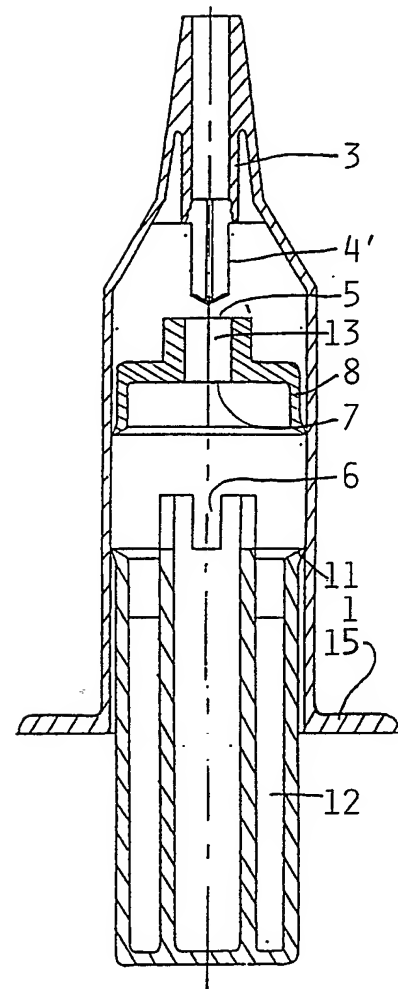


Fig. 2

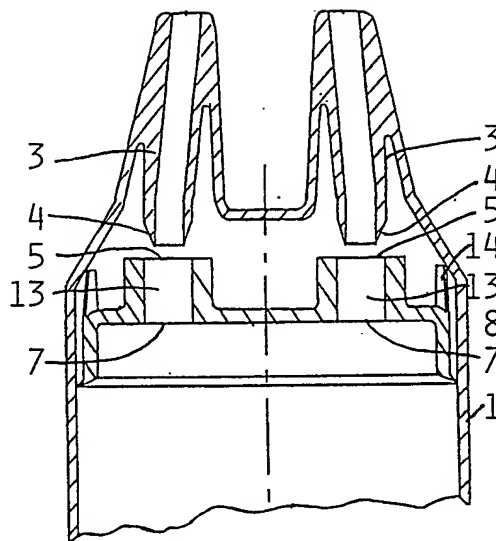


Fig. 3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK 92/00373

A. CLASSIFICATION OF SUBJECT MATTER

IPC5: A61M 15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC5: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE, A1, 4016126 (COSTER TECHNOLOGIE SPECIALI S.P.A.), 24 October 1991 (24.10.91), figures 8,16, abstract	6
A	--	1-5
A	US, A, 2672144 (M.J. COHEN), 16 March 1954 (16.03.54), figure 1	1-6
A	EP, A2, 0407276 (VALOIS), 9 January 1991 (09.01.91), figure 4	1-6
	--	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

4 March 1993

Date of mailing of the international search report

15 -03- 1993

Name and mailing address of the ISA/

Swedish Patent Office

Box 5055, S-102 42 STOCKHOLM

Facsimile No. +46 8 666 02 86

Authorized officer

Lena Nilsson

Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK 92/00373

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO, A1, 9106333 (NOVO NORDISK A/S), 16 May 1991 (16.05.91), figure 1, abstract --	1-6
X,P	WO, A1, 9206727 (NOVO NORDISK A/S), 30 April 1992 (30.04.92), figures 4,5	1-5
Y,P	 -- -----	6

INTERNATIONAL SEARCH REPORT

29/01/93

International application No.

PCT/DK 92/00373

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
DE-A1-	4016126	24/10/91	EP-A-	0452728	23/10/91
US-A-	2672144	16/03/54	NONE		
EP-A2-	0407276	09/01/91	CA-A-	2020425	05/01/91
			FR-A-	2649323	11/01/91
			JP-A-	3131271	04/06/91
WO-A1-	9106333	16/05/91	AU-A-	6617390	31/05/91
			CN-A-	1051304	15/05/91
			EP-A-	0499613	26/08/92
WO-A1-	9206727	30/04/92	AU-A-	8720791	20/05/92